

Operation News – January 2015



Roche acquires Trophos to expand its commitment in rare conditions with high medical need

- **Results from pivotal Phase II study suggest potential of olesoxime for treatment of patients with spinal muscular atrophy (SMA)**
- **US and EU regulatory authorities have granted orphan drug designation to olesoxime**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that it has agreed to acquire Trophos, a privately held biotechnology company based in Marseille, France. Trophos' proprietary screening platform generated olesoxime (TRO19622), which is being developed for SMA – a rare and debilitating genetic neuromuscular disease that is most commonly diagnosed in children. Results from a pivotal phase II clinical trial with olesoxime in SMA showed a beneficial effect on the maintenance of neuromuscular function in individuals with Type II and non-ambulatory Type III SMA, as well as a reduction in medical complications associated with the disease. These data were first presented in April 2014 at the annual meeting of the American Academy of Neurology (AAN).

"This acquisition highlights Roche's commitment to developing medicines for spinal muscular atrophy, a serious disease with no effective treatment," said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development at Roche. "We will build on the work done by Trophos and the French Muscular Dystrophy Association to advance the development of olesoxime and to bring it to people who live with this devastating condition as quickly as possible."

Under the terms of the agreement, Trophos' shareholders will receive an upfront cash payment of EUR 120 million, plus additional contingent payments of up to EUR 350 million based on achievement of certain predetermined milestones.

"SMA is a grievous disease with a huge impact on the daily life of patients and their families, who are currently left only with supportive care. We are proud to see the development of this medicine evolving, with the ultimate goal of a potential first medicine for SMA," said Christine

Placet, Chief Executive Officer of Trophos, and added, "this is a tremendous recognition of the work done by Trophos' teams and supporters over the past 16 years."

About Spinal Muscular Atrophy (SMA)

SMA is a life-limiting and highly disabling genetic disease characterized by progressive muscle weakness and loss of motor function. SMA affects the motor neurons of the voluntary muscles used for activities such as crawling, walking, head and neck control and swallowing. Typically, SMA presents in early childhood and is the most common genetic cause of infant mortality¹. It is one of the most common rare diseases, with one in 6,000 to one in 10,000 children affected. SMA is an autosomal recessive genetic disease caused by a loss of function of the *Survival Motor Neuron (SMN) 1* gene, which leads to insufficient levels of SMN protein, progressive deterioration of nerve cells in the spinal cord and loss of motor neurons. The mutated *SMN1* gene responsible for SMA is carried by up to 20 million potential parents in the United States and European Union, most of them unaware that they are carriers.

Patients with SMA are usually categorized by having one of the four types of the disease, based on severity, the highest level of motor functioning achieved and time of onset:

- Type I: The most severe form of SMA. Symptoms usually emerge within the first six months of life. Affected infants have low muscle tone, profound muscle weakness and impaired ability to move. Babies with type 1 SMA never sit. Simple tasks, such as holding up their heads, feeding and swallowing, can be very difficult. Progressive weakness of chest muscles increases the risk of respiratory infections and poor lung growth. Babies with type 1 SMA are at very high risk of irreversible decline in respiratory capacity. Type 1 SMA carries a high mortality rate, with more than half of all affected children not surviving beyond two years of age.
- Type II: Intermediate form of SMA. Symptoms usually emerge between six and 18 months of age. Individuals with Type II SMA typically are able to sit, but cannot walk, have severe and progressive motor disability and often require care 24 hours a day for their whole life. Individuals with Type 2 often develop severe curvature of the spine (scoliosis) and weakness of the chest muscles leading to high risk of severe respiratory infections. The severity and progression of the disease varies from person to person, life expectancy ranges from early childhood to adulthood.
- Type III: Symptoms can emerge anywhere between 18 months and early adulthood and include difficulty walking, muscle weakness and an increased risk of respiratory infections. A significant number of people with Type III SMA lose the ability to walk and can also develop severe scoliosis and other orthopedic problems. Many patients become non-ambulatory and are wheelchair bound at the age of 40.

Type IV: Adult form of SMA. A less common form of SMA, this type affects adults and is characterized by a slower progression of symptoms that mainly affect the ability to walk. Symptoms typically emerge after the age of 35 and patients have a normal life expectancy.

About Olesoxime

Olesoxime (TRO19622) is an investigational medicine designed to protect the health of motor nerve cells. Results of a pivotal phase II study of olesoxime in Type II and non-ambulatory Type III SMA patients from the ages of three to 25 years were first presented in April 2014 at the 66th American Academy of Neurology (AAN), Philadelphia, PA, USA. Trophos' development program was supported by the French Muscular Dystrophy Association. Olesoxime has been granted 'Orphan Medicinal Product' designation for the treatment of SMA by the European Medicines Agency and orphan drug designation by the US Food and Drug Administration.

About Trophos

Trophos is a clinical stage pharmaceutical company developing innovative therapeutics. The company has developed a proprietary cholesterol-oxime based chemistry platform. Trophos' mitochondrial targeted compounds enhance the function and survival of stressed cells by preventing mitochondrial permeability transition, a key determinant of cell death or survival.

Trophos was founded in 1999 and is based in Marseille, France. It is supported by a syndicate of private equity funds including ACG Management, OTC Agregator, Amundi Private Equity Funds, Turenne Capital, Sofipaca and Vesale Partners, as well as the French Muscular Dystrophy Association (AFM).

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

The transaction is subject to customary regulatory clearances including approval of the foreign investment by the French Ministry of Economy and expiration of the applicable Hart-Scott-Rodino waiting period. The transaction is anticipated to close in the first quarter of 2015.

ⁱ Society for Maternal-Fetal Medicine "Screening for spinal muscular atrophy not cost effective, study finds." Science Daily, last accessed Dec. 10, 2014